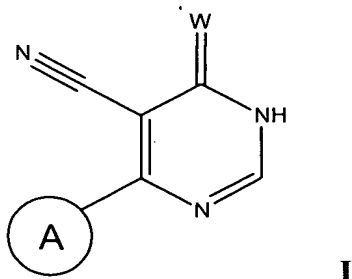


What is Claimed is:

1. A compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-NR^1C(O)N(R^1)_2$, $-NR^1CO_2R^1$, $-NR^1NR^1C(O)R^1$, $-NR^1NR^1C(O)N(R^1)_2$, $-NR^1NR^1CO_2R^1$, $-C(O)C(O)R^1$, $-C(O)CH_2C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-OC(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-S(O)R^1$, $-NR^1SO_2R^1$, $-NR^1SO_2N(R^1)_2$, $-C(=S)N(R^1)_2$, $-C(=NH)-N(R^1)_2$, $=O$, $=S$, $=NNHR^1$, $=NN(R^1)_2$, $=NNHC(O)R^1$, $=NNHCO_2(R^1)$, $=NNHSO_2(R^1)$, or $=NR^1$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-NR^2C(O)N(R^2)_2$, $-NR^2CO_2R^2$, $-NR^2NR^2C(O)R^2$, $-NR^2NR^2C(O)N(R^2)_2$, $-NR^2NR^2CO_2R^2$, $-C(O)C(O)R^2$, $-C(O)CH_2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-OC(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-S(O)R^2$, $-NR^2SO_2R^2$, $-NR^2SO_2N(R^2)_2$, $-C(=S)N(R^2)_2$, $-C(=NH)-N(R^2)_2$, $=O$, $=S$, $=NNHR^2$, $=NN(R^2)_2$, $=NNHC(O)R^2$, $=NNHCO_2(R^2)$, $=NNHSO_2(R^2)$, or $=NR^2$, wherein two independent occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl,

heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^3$, $-OR^3$, $-SR^3$, $-NO_2$, $-CN$, $-N(R^3)_2$, $-NR^3C(O)R^3$, $-NR^3C(O)N(R^3)_2$, $-NR^3CO_2R^3$, $-NR^3NR^3C(O)R^3$, $-NR^3NR^3C(O)N(R^3)_2$, $-NR^3NR^3CO_2R^3$, $-C(O)C(O)R^3$, $-C(O)CH_2C(O)R^3$, $-CO_2R^3$, $-C(O)R^3$, $-C(O)N(R^3)_2$, $-OC(O)N(R^3)_2$, $-S(O)_2R^3$, $-SO_2N(R^3)_2$, $-S(O)R^3$, $-NR^3SO_2R^3$, $-NR^3SO_2N(R^3)_2$, $-C(=S)N(R^3)_2$, $-C(=NH)-N(R^3)_2$, $=O$, $=S$, $=NNHR^3$, $=NN(R^3)_2$, $=NNHC(O)R^3$, $=NNHCO_2(R^3)$, $=NNHSO_2(R^3)$, or $=NR^3$; and

each R^3 is independently hydrogen or unsubstituted aliphatic;

provided that when ring A is phenyl, it must be substituted.

2. The compound of claim 1, wherein W is oxygen.

3. The compound of claim 1, wherein W is sulfur.

4. The compound of claim 2 or 3, ring A is phenyl substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-NR^1C(O)N(R^1)_2$, $-NR^1CO_2R^1$, $-NR^1NR^1C(O)R^1$, $-NR^1NR^1C(O)N(R^1)_2$, $-NR^1NR^1CO_2R^1$, $-C(O)C(O)R^1$, $-C(O)CH_2C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-OC(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-S(O)R^1$, $-NR^1SO_2R^1$, $-NR^1SO_2N(R^1)_2$, $-C(=S)N(R^1)_2$, or $-C(=NH)-N(R^1)_2$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 5-7-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-2 heteroatoms independently selected from N, O or S.

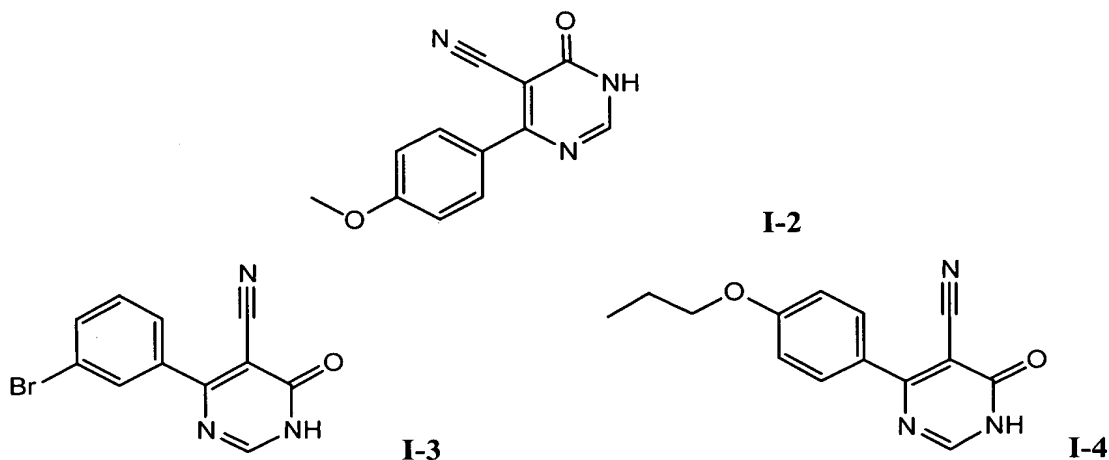
5. The compound of claim 4, wherein ring A is phenyl substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-NR^1SO_2R^1$, or $-C(=S)N(R^1)_2$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 5-7-membered heterocyclyl, aryl, or heteroaryl ring having 0-2 heteroatoms independently selected from N, O or S.

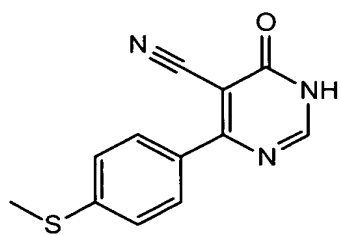
6. The compound of claim 2 or 3, wherein ring A is a 5-6 membered heterocyclyl or heteraryl ring having 1-2 heteroatoms independently selected from N, O or S, wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-NR^1SO_2R^1$, or $-C(=S)N(R^1)_2$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 5-7-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-2 heteroatoms independently selected from N, O or S.

7. The compound of claim 5, wherein ring A is naphthyl, benzodioxolyl, dihydrobenzodioxinyl, benzothiazolyl, benzoimidazolyl, or dihydrobenzo[b][1,4]dioxepinyl, wherein each member of ring A is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-NR^2SO_2R^2$, or $-C(=S)N(R^2)_2$.

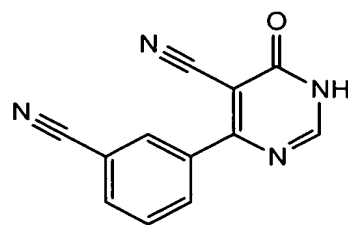
8. The compound of claim 6, wherein ring A is pyridinonyl, tetrahydroquinolinyl, pyridyl, or thiazolyl, wherein each member of ring A is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-NR^2SO_2R^2$, or $-C(=S)N(R^2)_2$.

9. The compound of claim 1, selected from:

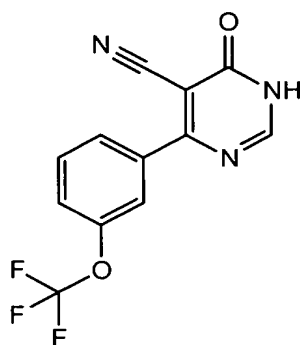




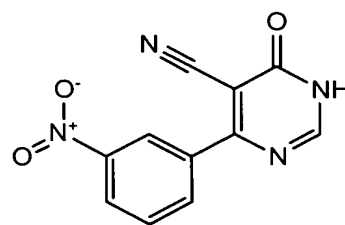
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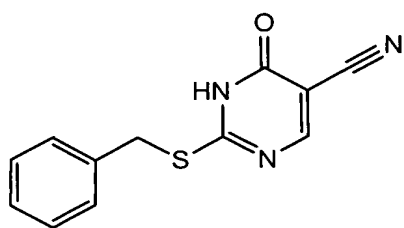
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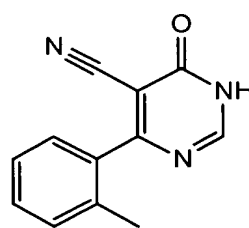
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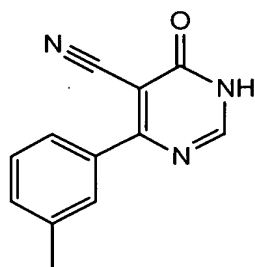
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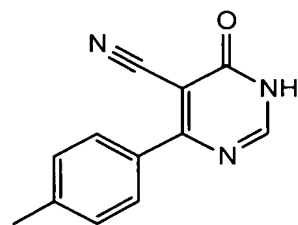
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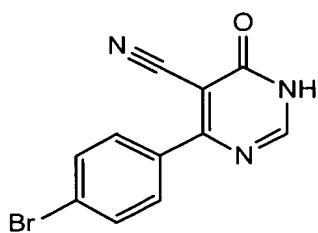
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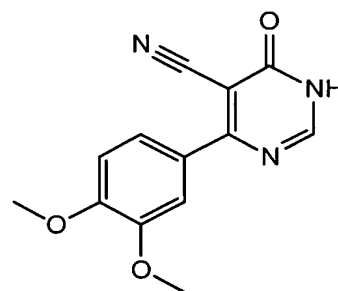
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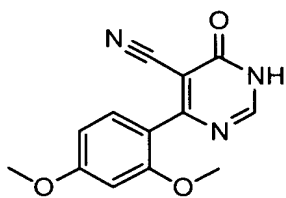
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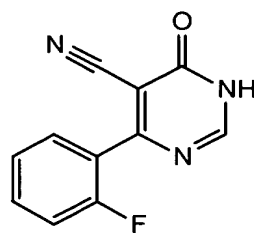
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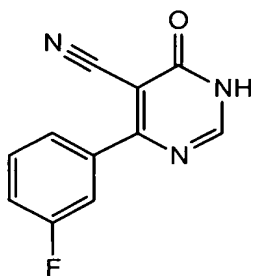
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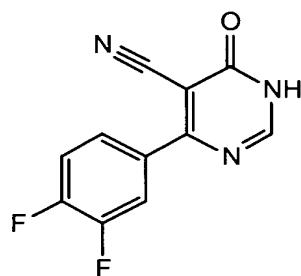
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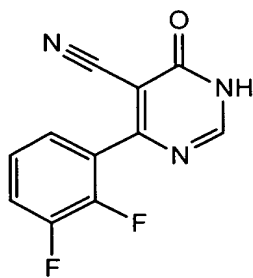
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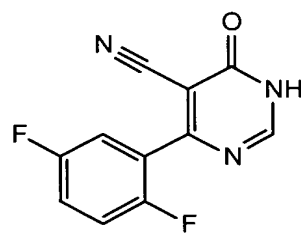
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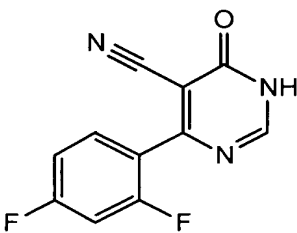
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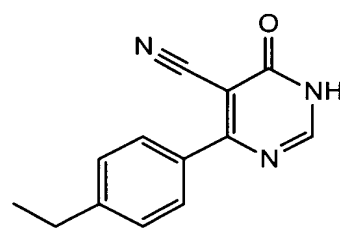
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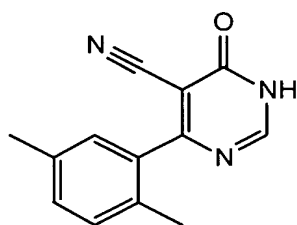
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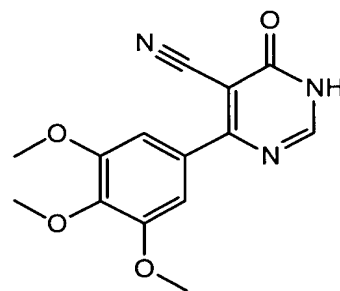
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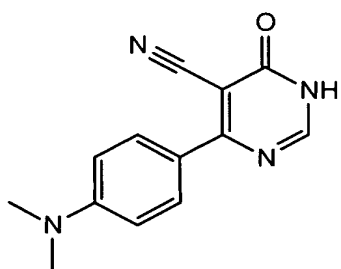
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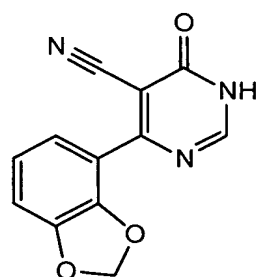
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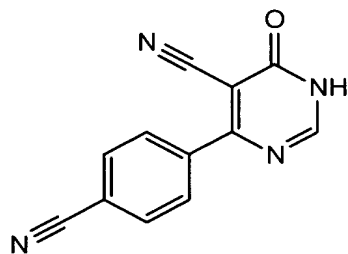
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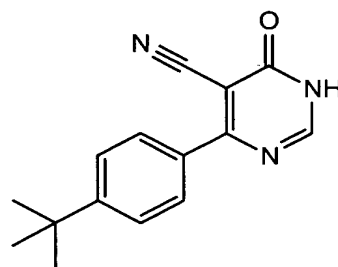
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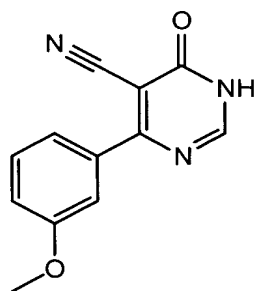
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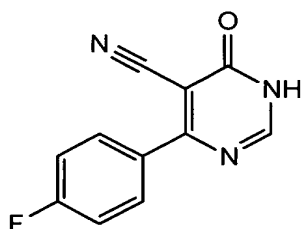
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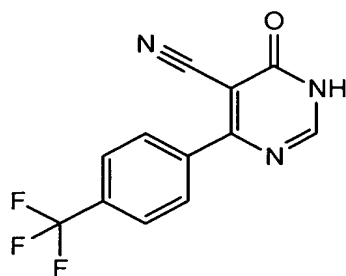
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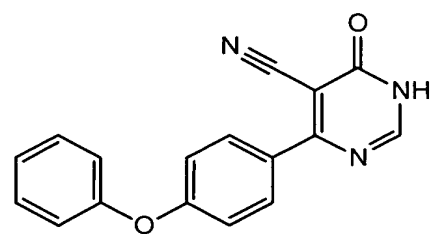
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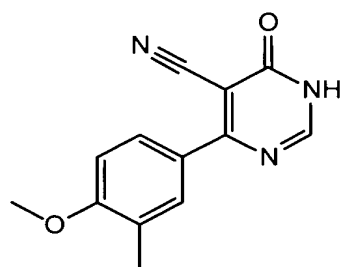
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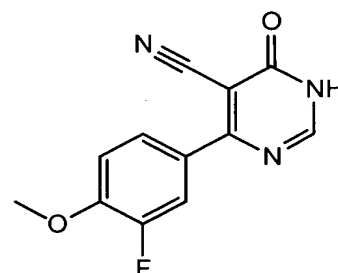
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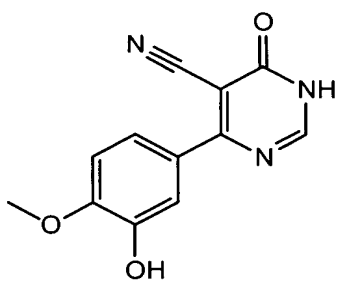
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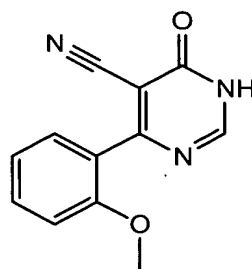
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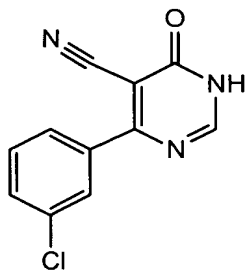
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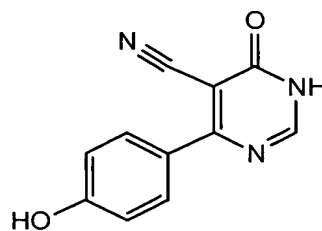
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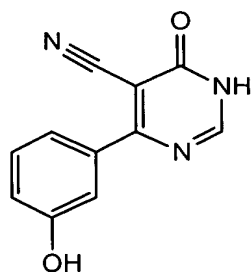
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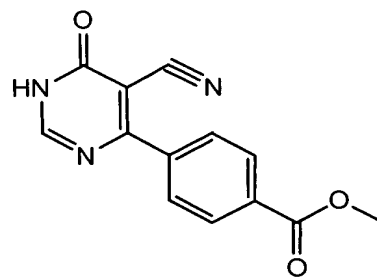
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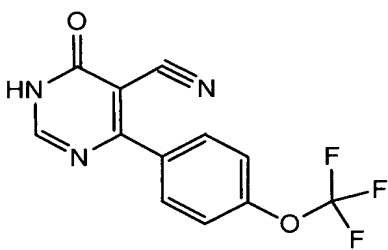
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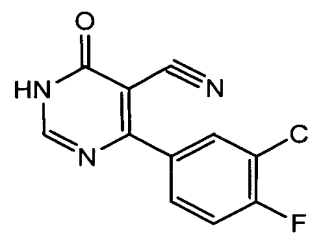
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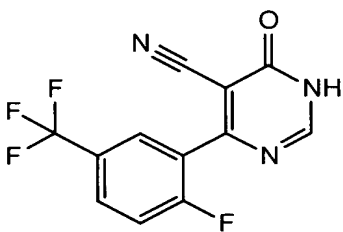
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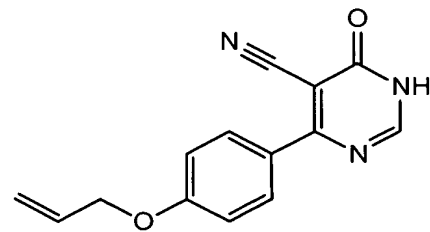
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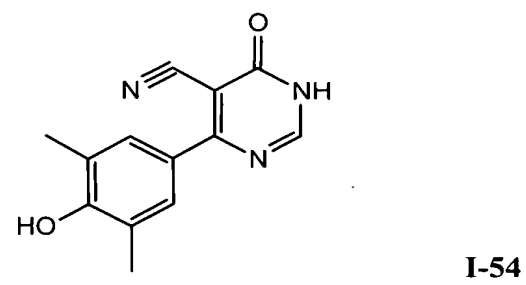
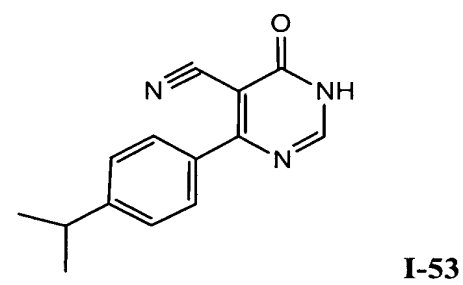
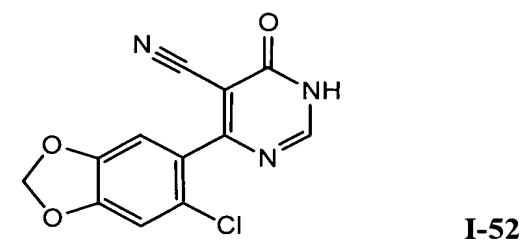
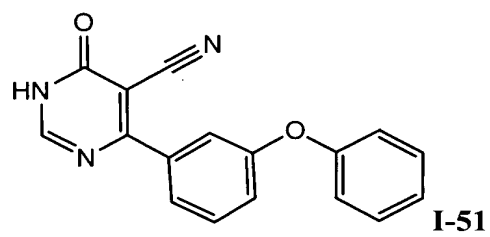
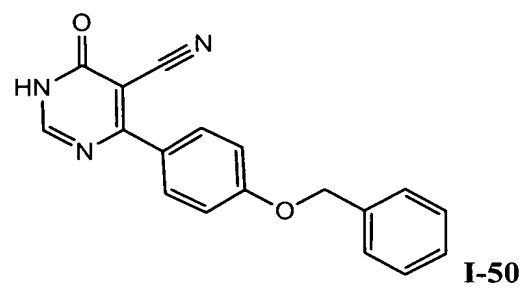
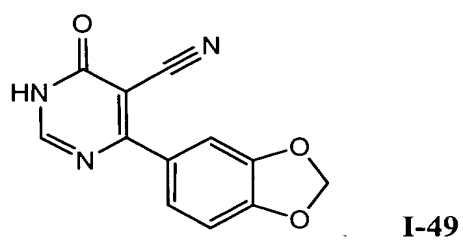
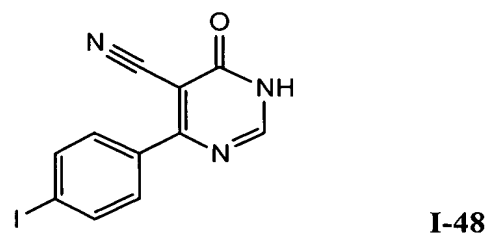
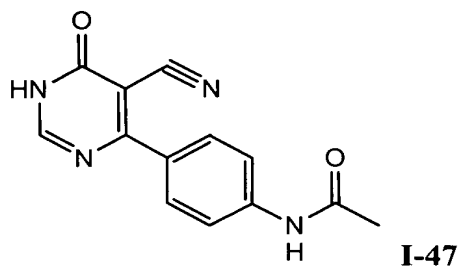
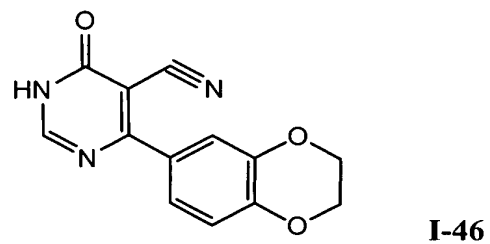
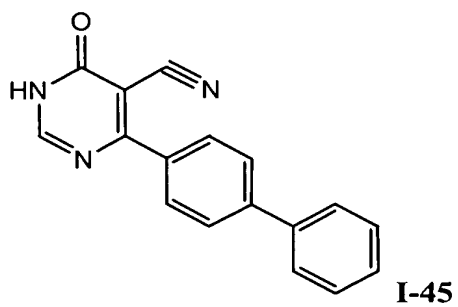
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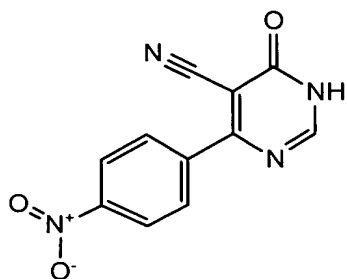
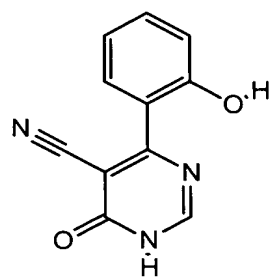
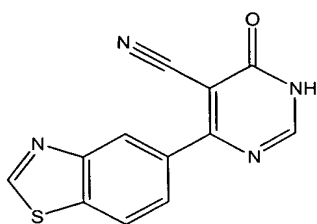
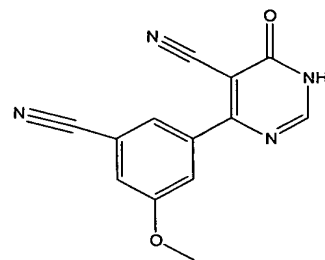
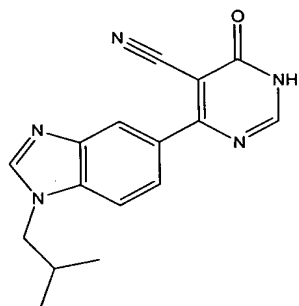
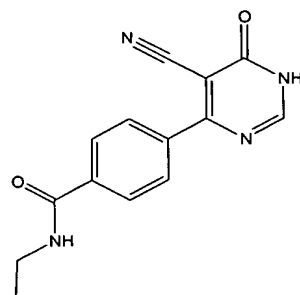
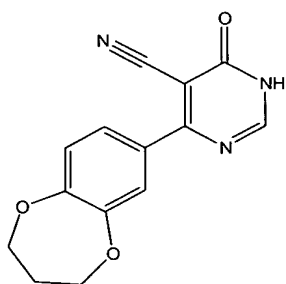
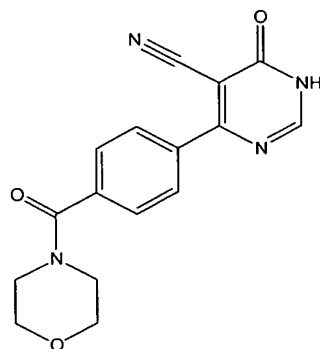
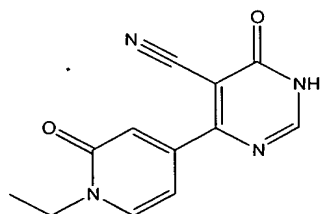
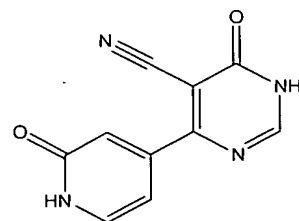


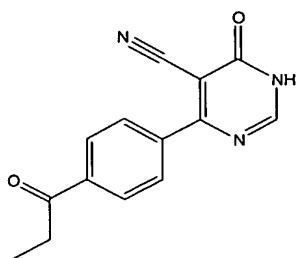
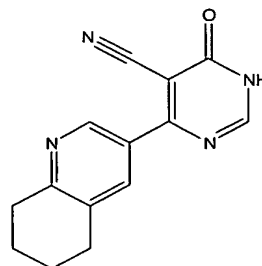
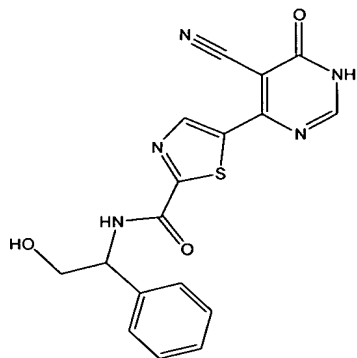
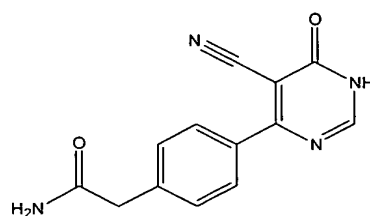
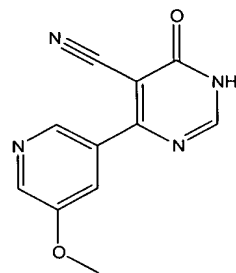
I-43



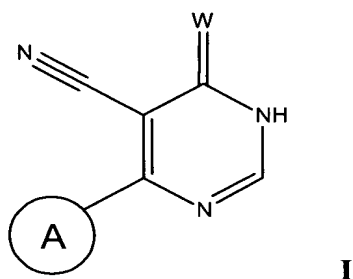
I-44



**I-55****I-56****I-57****I-58****I-59****I-60****I-61****I-62****I-63****I-64**

**I-65****I-66****I-67****I-68****I-69**

10. A composition comprising a compound of claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.
11. The composition of claim 9, additionally comprising a therapeutic agent selected from an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.
12. A method of inhibiting GSK-3 activity in:
 - (a) a patient in need thereof; or
 - (b) a biological sample;
 which method comprises administering to said patient, or contacting said biological sample with a compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-NR^1C(O)N(R^1)_2$, $-NR^1CO_2R^1$, $-NR^1NR^1C(O)R^1$, $-NR^1NR^1C(O)N(R^1)_2$, $-NR^1NR^1CO_2R^1$, $-C(O)C(O)R^1$, $-C(O)CH_2C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-OC(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-S(O)R^1$, $-NR^1SO_2R^1$, $-NR^1SO_2N(R^1)_2$, $-C(=S)N(R^1)_2$, $-C(=NH)-N(R^1)_2$, $=O$, $=S$, $=NNHR^1$, $=NN(R^1)_2$, $=NNHC(O)R^1$, $=NNHCO_2(R^1)$, $=NNHSO_2(R^1)$, or $=NR^1$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-NR^2C(O)N(R^2)_2$, $-NR^2CO_2R^2$, $-NR^2NR^2C(O)R^2$, $-NR^2NR^2C(O)N(R^2)_2$, $-NR^2NR^2CO_2R^2$, $-C(O)C(O)R^2$, $-C(O)CH_2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-OC(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-S(O)R^2$, $-NR^2SO_2R^2$, $-NR^2SO_2N(R^2)_2$, $-C(=S)N(R^2)_2$, $-C(=NH)-N(R^2)_2$, $=O$, $=S$, $=NNHR^2$, $=NN(R^2)_2$, $=NNHC(O)R^2$, $=NNHCO_2(R^2)$, $=NNHSO_2(R^2)$, or $=NR^2$, wherein two independent occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo,

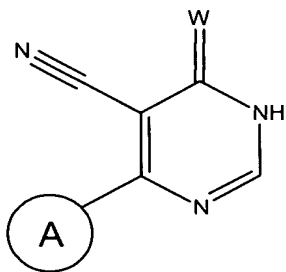
-R³, -OR³, -SR³, -NO₂, -CN, -N(R³)₂, -NR³C(O)R³, -NR³C(O)N(R³)₂, -NR³CO₂R³,
 -NR³NR³C(O)R³, -NR³NR³C(O)N(R³)₂, -NR³NR³CO₂R³, -C(O)C(O)R³, -C(O)CH₂C(O)R³,
 -CO₂R³, -C(O)R³, -C(O)N(R³)₂, -OC(O)N(R³)₂, -S(O)₂R³, -SO₂N(R³)₂, -S(O)R³, -NR³SO₂R³,
 -NR³SO₂N(R³)₂, -C(=S)N(R³)₂, -C(=NH)-N(R³)₂, =O, =S, =NNHR³, =NN(R³)₂,
 =NNHC(O)R³, =NNHCO₂(R³), =NNHSO₂(R³), or =NR³; and

each R³ is independently hydrogen or unsubstituted aliphatic; or

a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, adjuvant, or vehicle;

in an amount effective to inhibit GSK-3 activity.

13. A method of enhancing glycogen synthesis or lowering blood levels of glucose in a patient in need thereof, comprising administering to said patient a compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, -R¹, -OR¹, -SR¹, -NO₂, -CN, -N(R¹)₂, -NR¹C(O)R¹, -NR¹C(O)N(R¹)₂, -NR¹CO₂R¹,
 -NR¹NR¹C(O)R¹, -NR¹NR¹C(O)N(R¹)₂, -NR¹NR¹CO₂R¹, -C(O)C(O)R¹, -C(O)CH₂C(O)R¹,
 -CO₂R¹, -C(O)R¹, -C(O)N(R¹)₂, -OC(O)N(R¹)₂, -S(O)₂R¹, -SO₂N(R¹)₂, -S(O)R¹, -NR¹SO₂R¹,
 -NR¹SO₂N(R¹)₂, -C(=S)N(R¹)₂, -C(=NH)-N(R¹)₂, =O, =S, =NNHR¹, =NN(R¹)₂,
 =NNHC(O)R¹, =NNHCO₂(R¹), =NNHSO₂(R¹), or =NR¹, wherein two independent occurrences of R¹, on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R¹ group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-NR^2C(O)N(R^2)_2$, $-NR^2CO_2R^2$, $-NR^2NR^2C(O)R^2$, $-NR^2NR^2C(O)N(R^2)_2$, $-NR^2NR^2CO_2R^2$, $-C(O)C(O)R^2$, $-C(O)CH_2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-OC(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-S(O)R^2$, $-NR^2SO_2R^2$, $-NR^2SO_2N(R^2)_2$, $-C(=S)N(R^2)_2$, $-C(=NH)-N(R^2)_2$, $=O$, $=S$, $=NNHR^2$, $=NN(R^2)_2$, $=NNHC(O)R^2$, $=NNHCO_2(R^2)$, $=NNHSO_2(R^2)$, or $=NR^2$, wherein two independent occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

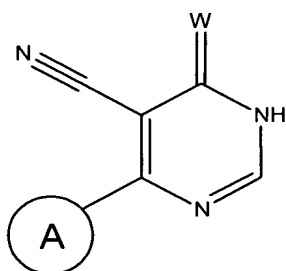
each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^3$, $-OR^3$, $-SR^3$, $-NO_2$, $-CN$, $-N(R^3)_2$, $-NR^3C(O)R^3$, $-NR^3C(O)N(R^3)_2$, $-NR^3CO_2R^3$, $-NR^3NR^3C(O)R^3$, $-NR^3NR^3C(O)N(R^3)_2$, $-NR^3NR^3CO_2R^3$, $-C(O)C(O)R^3$, $-C(O)CH_2C(O)R^3$, $-CO_2R^3$, $-C(O)R^3$, $-C(O)N(R^3)_2$, $-OC(O)N(R^3)_2$, $-S(O)_2R^3$, $-SO_2N(R^3)_2$, $-S(O)R^3$, $-NR^3SO_2R^3$, $-NR^3SO_2N(R^3)_2$, $-C(=S)N(R^3)_2$, $-C(=NH)-N(R^3)_2$, $=O$, $=S$, $=NNHR^3$, $=NN(R^3)_2$, $=NNHC(O)R^3$, $=NNHCO_2(R^3)$, $=NNHSO_2(R^3)$, or $=NR^3$; and

each R^3 is independently hydrogen or unsubstituted aliphatic; or

a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, adjuvant, or vehicle;

in an amount sufficient to enhance glycogen synthesis or lower blood glucose levels.

14. A method of inhibiting the production of hyperphosphorylated Tau protein in a patient in need thereof, comprising administering to said patient a compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-NR^1C(O)N(R^1)_2$, $-NR^1CO_2R^1$, $-NR^1NR^1C(O)R^1$, $-NR^1NR^1C(O)N(R^1)_2$, $-NR^1NR^1CO_2R^1$, $-C(O)C(O)R^1$, $-C(O)CH_2C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-OC(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-S(O)R^1$, $-NR^1SO_2R^1$, $-NR^1SO_2N(R^1)_2$, $-C(=S)N(R^1)_2$, $-C(=NH)-N(R^1)_2$, $=O$, $=S$, $=NNHR^1$, $=NN(R^1)_2$, $=NNHC(O)R^1$, $=NNHCO_2(R^1)$, $=NNHSO_2(R^1)$, or $=NR^1$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-NR^2C(O)N(R^2)_2$, $-NR^2CO_2R^2$, $-NR^2NR^2C(O)R^2$, $-NR^2NR^2C(O)N(R^2)_2$, $-NR^2NR^2CO_2R^2$, $-C(O)C(O)R^2$, $-C(O)CH_2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-OC(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-S(O)R^2$, $-NR^2SO_2R^2$, $-NR^2SO_2N(R^2)_2$, $-C(=S)N(R^2)_2$, $-C(=NH)-N(R^2)_2$, $=O$, $=S$, $=NNHR^2$, $=NN(R^2)_2$, $=NNHC(O)R^2$, $=NNHCO_2(R^2)$, $=NNHSO_2(R^2)$, or $=NR^2$, wherein two independent occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

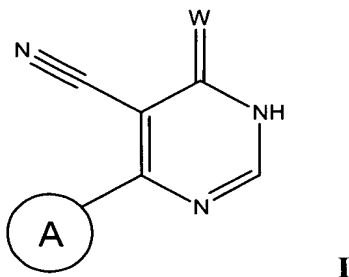
each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^2 except hydrogen is optionally substituted with halo, $-R^3$, $-OR^3$, $-SR^3$, $-NO_2$, $-CN$, $-N(R^3)_2$, $-NR^3C(O)R^3$, $-NR^3C(O)N(R^3)_2$, $-NR^3CO_2R^3$, $-NR^3NR^3C(O)R^3$, $-NR^3NR^3C(O)N(R^3)_2$, $-NR^3NR^3CO_2R^3$, $-C(O)C(O)R^3$, $-C(O)CH_2C(O)R^3$, $-CO_2R^3$, $-C(O)R^3$, $-C(O)N(R^3)_2$, $-OC(O)N(R^3)_2$, $-S(O)_2R^3$, $-SO_2N(R^3)_2$, $-S(O)R^3$, $-NR^3SO_2R^3$, $-NR^3SO_2N(R^3)_2$, $-C(=S)N(R^3)_2$, $-C(=NH)-N(R^3)_2$, $=O$, $=S$, $=NNHR^3$, $=NN(R^3)_2$, $=NNHC(O)R^3$, $=NNHCO_2(R^3)$, $=NNHSO_2(R^3)$, or $=NR^3$; and

each R^3 is independently hydrogen or unsubstituted aliphatic; or

a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, adjuvant, or vehicle;

in an amount sufficient to inhibit the production of hyperphosphorylated Tau protein.

15. A method of inhibiting the phosphorylation of β -catenin in a patient in need thereof, comprising administering to said patient a compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-NR^1C(O)N(R^1)_2$, $-NR^1CO_2R^1$, $-NR^1NR^1C(O)R^1$, $-NR^1NR^1C(O)N(R^1)_2$, $-NR^1NR^1CO_2R^1$, $-C(O)C(O)R^1$, $-C(O)CH_2C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-OC(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-S(O)R^1$, $-NR^1SO_2R^1$, $-NR^1SO_2N(R^1)_2$, $-C(=S)N(R^1)_2$, $-C(=NH)-N(R^1)_2$, $=O$, $=S$, $=NNHR^1$, $=NN(R^1)_2$, $=NNHC(O)R^1$, $=NNHCO_2(R^1)$, $=NNHSO_2(R^1)$, or $=NR^1$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-NR^2C(O)N(R^2)_2$, $-NR^2CO_2R^2$, $-NR^2NR^2C(O)R^2$, $-NR^2NR^2C(O)N(R^2)_2$, $-NR^2NR^2CO_2R^2$, $-C(O)C(O)R^2$, $-C(O)CH_2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-OC(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-S(O)R^2$, $-NR^2SO_2R^2$, $-NR^2SO_2N(R^2)_2$, $-C(=S)N(R^2)_2$, $-C(=NH)-N(R^2)_2$, $=O$, $=S$, $=NNHR^2$, $=NN(R^2)_2$, $=NNHC(O)R^2$, $=NNHCO_2(R^2)$, $=NNHSO_2(R^2)$, or $=NR^2$, wherein two independent

occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

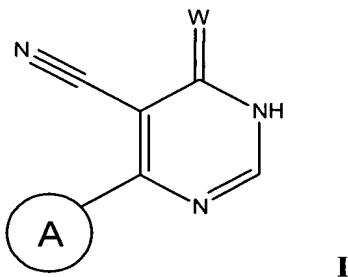
each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^3$, $-OR^3$, $-SR^3$, $-NO_2$, $-CN$, $-N(R^3)_2$, $-NR^3C(O)R^3$, $-NR^3C(O)N(R^3)_2$, $-NR^3CO_2R^3$, $-NR^3NR^3C(O)R^3$, $-NR^3NR^3C(O)N(R^3)_2$, $-NR^3NR^3CO_2R^3$, $-C(O)C(O)R^3$, $-C(O)CH_2C(O)R^3$, $-CO_2R^3$, $-C(O)R^3$, $-C(O)N(R^3)_2$, $-OC(O)N(R^3)_2$, $-S(O)_2R^3$, $-SO_2N(R^3)_2$, $-S(O)R^3$, $-NR^3SO_2R^3$, $-NR^3SO_2N(R^3)_2$, $-C(=S)N(R^3)_2$, $-C(=NH)-N(R^3)_2$, $=O$, $=S$, $=NNHR^3$, $=NN(R^3)_2$, $=NNHC(O)R^3$, $=NNHCO_2(R^3)$, $=NNHSO_2(R^3)$, or $=NR^3$; and

each R^3 is independently hydrogen or unsubstituted aliphatic; or

a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, adjuvant, or vehicle;

in an amount sufficient to inhibit phosphorylation of β -catenin.

16. A method of treating or lessening the severity of a disease or condition selected from a cardiac disorder, a neurodegenerative disorder, an autoimmune disorder, an inflammatory disorder, an immunologically mediated disorder, or a metabolic disorder, comprising administering to a patient a compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-NR^1C(O)N(R^1)_2$, $-NR^1CO_2R^1$, $-NR^1NR^1C(O)R^1$, $-NR^1NR^1C(O)N(R^1)_2$, $-NR^1NR^1CO_2R^1$, $-C(O)C(O)R^1$, $-C(O)CH_2C(O)R^1$,

$-\text{CO}_2\text{R}^1$, $-\text{C}(\text{O})\text{R}^1$, $-\text{C}(\text{O})\text{N}(\text{R}^1)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^1)_2$, $-\text{S}(\text{O})_2\text{R}^1$, $-\text{SO}_2\text{N}(\text{R}^1)_2$, $-\text{S}(\text{O})\text{R}^1$, $-\text{NR}^1\text{SO}_2\text{R}^1$, $-\text{NR}^1\text{SO}_2\text{N}(\text{R}^1)_2$, $-\text{C}(=\text{S})\text{N}(\text{R}^1)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^1)_2$, $=\text{O}$, $=\text{S}$, $=\text{NNHR}^1$, $=\text{NN}(\text{R}^1)_2$, $=\text{NNHC}(\text{O})\text{R}^1$, $=\text{NNHCO}_2(\text{R}^1)$, $=\text{NNHSO}_2(\text{R}^1)$, or $=\text{NR}^1$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-\text{R}^2$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{NO}_2$, $-\text{CN}$, $-\text{N}(\text{R}^2)_2$, $-\text{NR}^2\text{C}(\text{O})\text{R}^2$, $-\text{NR}^2\text{C}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{NR}^2\text{CO}_2\text{R}^2$, $-\text{NR}^2\text{NR}^2\text{C}(\text{O})\text{R}^2$, $-\text{NR}^2\text{NR}^2\text{C}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{NR}^2\text{NR}^2\text{CO}_2\text{R}^2$, $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^2$, $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^2$, $-\text{CO}_2\text{R}^2$, $-\text{C}(\text{O})\text{R}^2$, $-\text{C}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{S}(\text{O})_2\text{R}^2$, $-\text{SO}_2\text{N}(\text{R}^2)_2$, $-\text{S}(\text{O})\text{R}^2$, $-\text{NR}^2\text{SO}_2\text{R}^2$, $-\text{NR}^2\text{SO}_2\text{N}(\text{R}^2)_2$, $-\text{C}(=\text{S})\text{N}(\text{R}^2)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^2)_2$, $=\text{O}$, $=\text{S}$, $=\text{NNHR}^2$, $=\text{NN}(\text{R}^2)_2$, $=\text{NNHC}(\text{O})\text{R}^2$, $=\text{NNHCO}_2(\text{R}^2)$, $=\text{NNHSO}_2(\text{R}^2)$, or $=\text{NR}^2$, wherein two independent occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

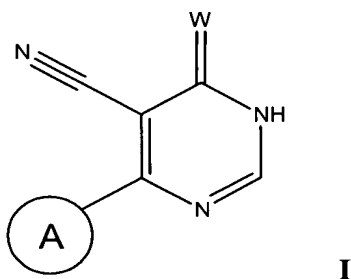
each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^2 except hydrogen is optionally substituted with halo, $-\text{R}^3$, $-\text{OR}^3$, $-\text{SR}^3$, $-\text{NO}_2$, $-\text{CN}$, $-\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{C}(\text{O})\text{R}^3$, $-\text{NR}^3\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{CO}_2\text{R}^3$, $-\text{NR}^3\text{NR}^3\text{C}(\text{O})\text{R}^3$, $-\text{NR}^3\text{NR}^3\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{NR}^3\text{CO}_2\text{R}^3$, $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^3$, $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^3$, $-\text{CO}_2\text{R}^3$, $-\text{C}(\text{O})\text{R}^3$, $-\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{S}(\text{O})_2\text{R}^3$, $-\text{SO}_2\text{N}(\text{R}^3)_2$, $-\text{S}(\text{O})\text{R}^3$, $-\text{NR}^3\text{SO}_2\text{R}^3$, $-\text{NR}^3\text{SO}_2\text{N}(\text{R}^3)_2$, $-\text{C}(=\text{S})\text{N}(\text{R}^3)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^3)_2$, $=\text{O}$, $=\text{S}$, $=\text{NNHR}^3$, $=\text{NN}(\text{R}^3)_2$, $=\text{NNHC}(\text{O})\text{R}^3$, $=\text{NNHCO}_2(\text{R}^3)$, $=\text{NNHSO}_2(\text{R}^3)$, or $=\text{NR}^3$; and

each R^3 is independently hydrogen or unsubstituted aliphatic; or

a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, adjuvant, or vehicle;

in an amount effective to treat or lessen the severity of said disease or condition.

17. A method of treating or lessening the severity of a disease or condition selected from allergy, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS-associated dementia, amyotrophic lateral sclerosis (AML, Lou Gehrig's disease), multiple sclerosis (MS), schizophrenia, cardiomyocyte hypertrophy, reperfusion/ischemia, or baldness, comprising administering to a patient a compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-R^1$, $-OR^1$, $-SR^1$, $-NO_2$, $-CN$, $-N(R^1)_2$, $-NR^1C(O)R^1$, $-NR^1C(O)N(R^1)_2$, $-NR^1CO_2R^1$, $-NR^1NR^1C(O)R^1$, $-NR^1NR^1C(O)N(R^1)_2$, $-NR^1NR^1CO_2R^1$, $-C(O)C(O)R^1$, $-C(O)CH_2C(O)R^1$, $-CO_2R^1$, $-C(O)R^1$, $-C(O)N(R^1)_2$, $-OC(O)N(R^1)_2$, $-S(O)_2R^1$, $-SO_2N(R^1)_2$, $-S(O)R^1$, $-NR^1SO_2R^1$, $-NR^1SO_2N(R^1)_2$, $-C(=S)N(R^1)_2$, $-C(=NH)-N(R^1)_2$, $=O$, $=S$, $=NNHR^1$, $=NN(R^1)_2$, $=NNHC(O)R^1$, $=NNHCO_2(R^1)$, $=NNHSO_2(R^1)$, or $=NR^1$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-R^2$, $-OR^2$, $-SR^2$, $-NO_2$, $-CN$, $-N(R^2)_2$, $-NR^2C(O)R^2$, $-NR^2C(O)N(R^2)_2$, $-NR^2CO_2R^2$, $-NR^2NR^2C(O)R^2$, $-NR^2NR^2C(O)N(R^2)_2$, $-NR^2NR^2CO_2R^2$, $-C(O)C(O)R^2$, $-C(O)CH_2C(O)R^2$, $-CO_2R^2$, $-C(O)R^2$, $-C(O)N(R^2)_2$, $-OC(O)N(R^2)_2$, $-S(O)_2R^2$, $-SO_2N(R^2)_2$, $-S(O)R^2$, $-NR^2SO_2R^2$, $-NR^2SO_2N(R^2)_2$, $-C(=S)N(R^2)_2$, $-C(=NH)-N(R^2)_2$, $=O$, $=S$, $=NNHR^2$, $=NN(R^2)_2$,

$=\text{NNHC}(\text{O})\text{R}^2$, $=\text{NNHCO}_2(\text{R}^2)$, $=\text{NNHSO}_2(\text{R}^2)$, or $=\text{NR}^2$, wherein two independent occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

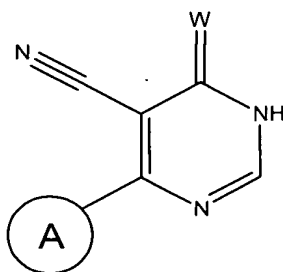
each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-\text{R}^3$, $-\text{OR}^3$, $-\text{SR}^3$, $-\text{NO}_2$, $-\text{CN}$, $-\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{C}(\text{O})\text{R}^3$, $-\text{NR}^3\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{CO}_2\text{R}^3$, $-\text{NR}^3\text{NR}^3\text{C}(\text{O})\text{R}^3$, $-\text{NR}^3\text{NR}^3\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{NR}^3\text{CO}_2\text{R}^3$, $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^3$, $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^3$, $-\text{CO}_2\text{R}^3$, $-\text{C}(\text{O})\text{R}^3$, $-\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{S}(\text{O})_2\text{R}^3$, $-\text{SO}_2\text{N}(\text{R}^3)_2$, $-\text{S}(\text{O})\text{R}^3$, $-\text{NR}^3\text{SO}_2\text{R}^3$, $-\text{NR}^3\text{SO}_2\text{N}(\text{R}^3)_2$, $-\text{C}(=\text{S})\text{N}(\text{R}^3)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^3)_2$, $=\text{O}$, $=\text{S}$, $=\text{NNHR}^3$, $=\text{NN}(\text{R}^3)_2$, $=\text{NNHC}(\text{O})\text{R}^3$, $=\text{NNHCO}_2(\text{R}^3)$, $=\text{NNHSO}_2(\text{R}^3)$, or $=\text{NR}^3$; and

each R^3 is independently hydrogen or unsubstituted aliphatic; or

a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, adjuvant, or vehicle;

in an amount effective to treat or lessen the severity of said disease or condition.

18. A method of treating or lessening the severity of stroke in a patient, comprising administering to said patient a compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

W is oxygen or sulfur;

ring A is a 5-6 membered aryl, heterocyclyl or heteroaryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

wherein ring A is optionally substituted with 1-4 groups independently selected from halo, $-\text{R}^1$, $-\text{OR}^1$, $-\text{SR}^1$, $-\text{NO}_2$, $-\text{CN}$, $-\text{N}(\text{R}^1)_2$, $-\text{NR}^1\text{C}(\text{O})\text{R}^1$, $-\text{NR}^1\text{C}(\text{O})\text{N}(\text{R}^1)_2$, $-\text{NR}^1\text{CO}_2\text{R}^1$, $-\text{NR}^1\text{NR}^1\text{C}(\text{O})\text{R}^1$, $-\text{NR}^1\text{NR}^1\text{C}(\text{O})\text{N}(\text{R}^1)_2$, $-\text{NR}^1\text{NR}^1\text{CO}_2\text{R}^1$, $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^1$, $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^1$, $-\text{CO}_2\text{R}^1$, $-\text{C}(\text{O})\text{R}^1$, $-\text{C}(\text{O})\text{N}(\text{R}^1)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^1)_2$, $-\text{S}(\text{O})_2\text{R}^1$, $-\text{SO}_2\text{N}(\text{R}^1)_2$, $-\text{S}(\text{O})\text{R}^1$, $-\text{NR}^1\text{SO}_2\text{R}^1$,

$-\text{NR}^1\text{SO}_2\text{N}(\text{R}^1)_2$, $-\text{C}(=\text{S})\text{N}(\text{R}^1)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^1)_2$, $=\text{O}$, $=\text{S}$, $=\text{NNHR}^1$, $=\text{NN}(\text{R}^1)_2$, $=\text{NNHC}(\text{O})\text{R}^1$, $=\text{NNHCO}_2(\text{R}^1)$, $=\text{NNHSO}_2(\text{R}^1)$, or $=\text{NR}^1$, wherein two independent occurrences of R^1 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^1 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^1 except hydrogen is optionally substituted with halo, $-\text{R}^2$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{NO}_2$, $-\text{CN}$, $-\text{N}(\text{R}^2)_2$, $-\text{NR}^2\text{C}(\text{O})\text{R}^2$, $-\text{NR}^2\text{C}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{NR}^2\text{CO}_2\text{R}^2$, $-\text{NR}^2\text{NR}^2\text{C}(\text{O})\text{R}^2$, $-\text{NR}^2\text{NR}^2\text{C}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{NR}^2\text{NR}^2\text{CO}_2\text{R}^2$, $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^2$, $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^2$, $-\text{CO}_2\text{R}^2$, $-\text{C}(\text{O})\text{R}^2$, $-\text{C}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^2)_2$, $-\text{S}(\text{O})_2\text{R}^2$, $-\text{SO}_2\text{N}(\text{R}^2)_2$, $-\text{S}(\text{O})\text{R}^2$, $-\text{NR}^2\text{SO}_2\text{R}^2$, $-\text{NR}^2\text{SO}_2\text{N}(\text{R}^2)_2$, $-\text{C}(=\text{S})\text{N}(\text{R}^2)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^2)_2$, $=\text{O}$, $=\text{S}$, $=\text{NNHR}^2$, $=\text{NN}(\text{R}^2)_2$, $=\text{NNHC}(\text{O})\text{R}^2$, $=\text{NNHCO}_2(\text{R}^2)$, $=\text{NNHSO}_2(\text{R}^2)$, or $=\text{NR}^2$, wherein two independent occurrences of R^2 , on the same substituent or different substituents, optionally taken together with the atom or atoms to which each R^2 group is bound, form a 3-8-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

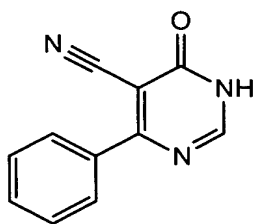
each R^2 is independently selected from hydrogen, aliphatic, aryl, heteroaryl or heterocyclyl, wherein each member of R^2 except hydrogen is optionally substituted with halo, $-\text{R}^3$, $-\text{OR}^3$, $-\text{SR}^3$, $-\text{NO}_2$, $-\text{CN}$, $-\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{C}(\text{O})\text{R}^3$, $-\text{NR}^3\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{CO}_2\text{R}^3$, $-\text{NR}^3\text{NR}^3\text{C}(\text{O})\text{R}^3$, $-\text{NR}^3\text{NR}^3\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{NR}^3\text{NR}^3\text{CO}_2\text{R}^3$, $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^3$, $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^3$, $-\text{CO}_2\text{R}^3$, $-\text{C}(\text{O})\text{R}^3$, $-\text{C}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{OC}(\text{O})\text{N}(\text{R}^3)_2$, $-\text{S}(\text{O})_2\text{R}^3$, $-\text{SO}_2\text{N}(\text{R}^3)_2$, $-\text{S}(\text{O})\text{R}^3$, $-\text{NR}^3\text{SO}_2\text{R}^3$, $-\text{NR}^3\text{SO}_2\text{N}(\text{R}^3)_2$, $-\text{C}(=\text{S})\text{N}(\text{R}^3)_2$, $-\text{C}(=\text{NH})-\text{N}(\text{R}^3)_2$, $=\text{O}$, $=\text{S}$, $=\text{NNHR}^3$, $=\text{NN}(\text{R}^3)_2$, $=\text{NNHC}(\text{O})\text{R}^3$, $=\text{NNHCO}_2(\text{R}^3)$, $=\text{NNHSO}_2(\text{R}^3)$, or $=\text{NR}^3$; and

each R^3 is independently hydrogen or unsubstituted aliphatic; or

a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier, adjuvant, or vehicle;

in an amount effective to treat or lessen the severity of stroke in said patient.

19. The method according to any one of claims 12-18, wherein said method comprises administering to said patient a compound of claim 8 or compound **I-1**:

**I-1** .

20. The method according to any one of claims 12-18, comprising the additional step of administering to said patient an additional therapeutic agent selected from an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and

said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.